

Application No.: 09/840,008
Filing Date: April 20, 2001
Amendment in Response to Notice to Comply (mailed 02/25/03) mailed 06/25/03
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Attorney Docket No.: SALK2270-4
(088802-5211)



Amendments to the Specification

Please replace the previous Sequence Listing with the new Sequence Listing submitted herewith.

Please insert the following acknowledgment and heading therefor after the title on page 1 of the specification as filed:

--ACKNOWLEDGMENT

Q2 This invention was made with United States Government support under Grant No. DK57978, awarded by the National Institutes of Health. The Government has certain rights in the invention.--

Please replace paragraph [0034] with the following replacement paragraph.

Q3 -- [0034] **Figure 6A (SEQ ID NOs: 3-11, respectively, in order of appearance)** presents a schematic comparison of nucleotide sequences encoding response elements found in inducible cytochrome P450 enzymes. A database search for repeats of the sequence RGKTCA (SEQ ID NO: 41) was performed and some of the matches for enzymes involved in hepatic steroid hydroxylation are indicated. The standard nomenclature for P450 enzymes has been utilized. P450R is the single P450 oxidoreductase required for hydroxylation of steroids. UGT1A6 is a rat uridine diphosphate (UDP)-glucuronosyltransferase that conjugates glucuronic acid to hydroxylated steroids. --

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Please replace paragraph [0035] with the following replacement paragraph.

bx
-- [0035] **Figure 6B (SEQ ID NOs: 33-35, respectively, in order of appearance)** presents a schematic comparison of conserved glucocorticoid-response elements found in human CYP3 genes. The region of human CYP3A4 shown is necessary and sufficient for glucocorticoid and rifampicin induction of the full-length promoter. Corresponding regions of CYP3A5 and CYP3A7 are shown (Barwick *et al.*, *Mol. Pharmacol.* 50:10-16, 1996). --

Please replace paragraph [0042] with the following replacement paragraph.

bx
-- [0042] **Figure 8C** illustrates that the DR-3 element is essential for SXR-mediated activation of CYP3A23, and is interchangeable with the IR-6 element. The wild type (DR3/WT, SEQ ID NO: 39, filled bars) or mutant forms (DR3/M1, SEQ ID NO: 42, open bars; DR3/M2, **SEQ ID NO: 43**, stippled bars; and DR3/IR6, **SEQ ID NO: 24** **SEQ ID NO: 43**, hatched bars) of CYP3A23 cellular promoter reporters were transfected into primary rat hepatocytes in the presence of expression vector for SXR. The ligand treatment and data presentation are the same as in Figure 8A. RIF, rifampicin; CTZ, clotrimazole. Note the disruptions of DR-3 element (DR3/M1, and DR3/M2) abrogate the activation of CYP3A23, and the replacement of DR-3 element with IR-6 element (DR3/IR3) rescues the responsiveness. --

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Please replace paragraph [0067] with the following replacement paragraph.

--[0067] Examples of response elements suitable for use in practice of the invention methods can be selected from the following:

DR-3,4,5 = AGGTCANnAGGTCA, wherein n is 3, 4, or 5 (**SEQ ID NOS: 15, 16, and 17 (SEQ ID NO: 44);**

β DR-3,4,5 = AGTTCANnTGAAC, wherein n is 3, 4 or 5 (SEQ ID NO: 22); and

IR-6 = TGAACTNnAGGTCA, wherein n is 6 (SEQ ID NO: 23), and the like.--
